COLD ATMOSPHERIC PRESSURE PLASMA-ACTIVATED LIQUIDS FOR CANCER TREATMENT

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With the promising perspective of becoming a new type of oncological therapy, low-temperature plasma (LTP) has recently gained much attention [1,2]. The liquids treated with LTP contain a variety of reactive species, including molecular, atomic, radical, and ionic compounds. These interactions are changing the chemical properties of the irradiated liquids, reported to have anti-cancer activity [3, 4]. Chemically active species identified in various plasma-treated liquids, such as Ringer's lactate, chitosan, or cyclodextrins depend on the irradiation time and on the feeding gas mixture (argon, nitrogen, and oxygen) used in the discharge. The degree of polymerization is also modified by plasma treatment, depending on the chemical composition of the initial compounds used in the experiments.

The cleavage of radicals from the liquid precursors, such as methyl radicals, is followed by the formation of key intermediate products (peracetic acid, 2-2-dihydroxyacetic acid, or carboxymethyl radicals). Further interactions in plasma result in the formation of more complex compounds, such as glyceric acid, acetic anhydride, ethyl acetate, or tricarballylic acid with stimulatory or inhibitory effects on cell viability. The killing selectivity towards cancer cells is influenced by the gas mixture used in the discharge, but also by the chemical composition of liquids, higher molecular weight compounds used in our studies being very effective in destroying the cancer cells. Plasma is generating a mixture of certain chemically active species in the exact amount able to induce cytotoxic effects on breast cancer cell lines (MCF-7), leaving the non-tumorigenic epithelial cell lines (MCF-10A) unharmed. The adjustment of the plasma parameters gives the possibility of engineering liquids that induce a selective generation of chemical compounds responsible for the antitumor activity.

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References

 S. Toyokuni, Y. Ikehara, F. Kikkawa, and M. Hori, *Plasma medical science* (AP, Elsevier, 2018)
Y. Liu, K. Ishikawa, C. Miron, H. Hashizume, H. Tanaka, and M. Hori, *Plasma Sources Sci. Technol.*, **30** (2021) 04LT03
D. Ito, N. Iwata, K. Ishikawa, K. Nakamura, H. Hashizume, C. Miron, H. Tanaka, H. Kajiyama, S. Toyokuni, M. Mizuno, and M. Hori, Appl. Phys. Express, **15** (2022) 056001
H. Tanaka, M. Mizuno, K. Ishikawa, C. Miron, Y. Okazaki, S. Toyokuni, K. Nakamura, H. Kajiyama, M. Hori, Free Radical Research (2023) <u>https://doi.org/10.1080/10715762.2023.2182663</u>